Epidemiology and Impact of Herpes Zoster and Postherpetic Neuralgia in Older Adults

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Objectives

- To review the incidence, prevalence and risk factors for herpes zoster and postherpetic neuralgia
- To discuss the impact of herpes zoster and postherpetic neuralgia on older adults

Photo provided courtesy of Dr. Kenneth Schmader, Duke University and Durham VA Medical Centers

Incidence of Herpes Zoster

- About 1 million cases in the US annually
- 1.2 to 4.8 cases per 1000 person-years in adults of all ages
- 7.2 to 11.8 cases per 1000 person-years in adults 60 years of age and older

Gnann J et al. N Engl J Med. 2002;347:340-346; Thomas SL et al. Lancet Infect Dis 2004;4:26-33; Oxman et al. NEJM. 2005;352:2271-84

Incidence of Herpes Zoster

- **Shingles Prevention Study Placebo Group (n = 19,247) adults ≥ 60 years old**
  - **Prospective active surveillance**
  - **94% cases microbiologically confirmed**
  - **Incidence = 11.1 cases per 1000 person-years**

Lifetime Risk of Herpes Zoster

- **Lifetime risk of herpes zoster estimated at 20-30%**
- **50% of individuals living until 85 years of age will ultimately develop herpes zoster**

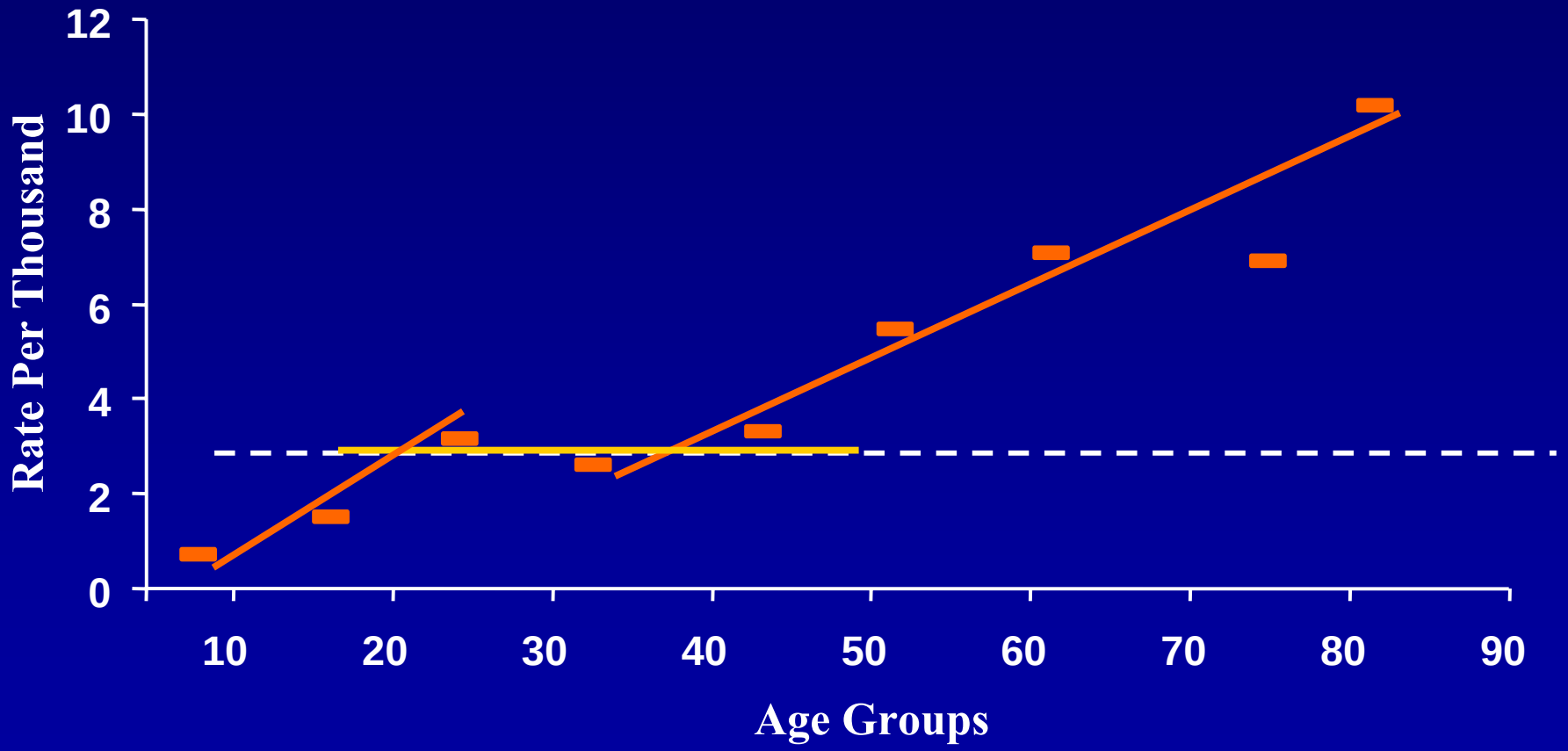
Gnann J et al. N Engl J Med. 2002;347:340-346.
Katz J et al. Clin Infect Dis. 2004;39:342-348.
Ragozzino M et al. Medicine. 1982;61:310-316.

Increasing Age and Cellular Immunosuppression are the Main Risk Factors for Herpes Zoster

- The number of herpes zoster cases highest among immunocompetent older adults
- As population ages, the absolute number of herpes zoster cases will increase

Thomas SL et al. Lancet Infect Dis 2004;4:26-33; Schmader, KE. In: Varicella-Zoster Virus, Arvin&Gershon, eds. Cambridge University Press 2000:2220-246

Age and Incidence of Herpes Zoster



Hope-Simpson RE. Proc R Soc Med 1965;58:9-20

Age- specific Incidence of Zoster

Age-Specific Incidence Rates of Herpes Zoster, Group Health Cooperative in Washington State, 1992-2002

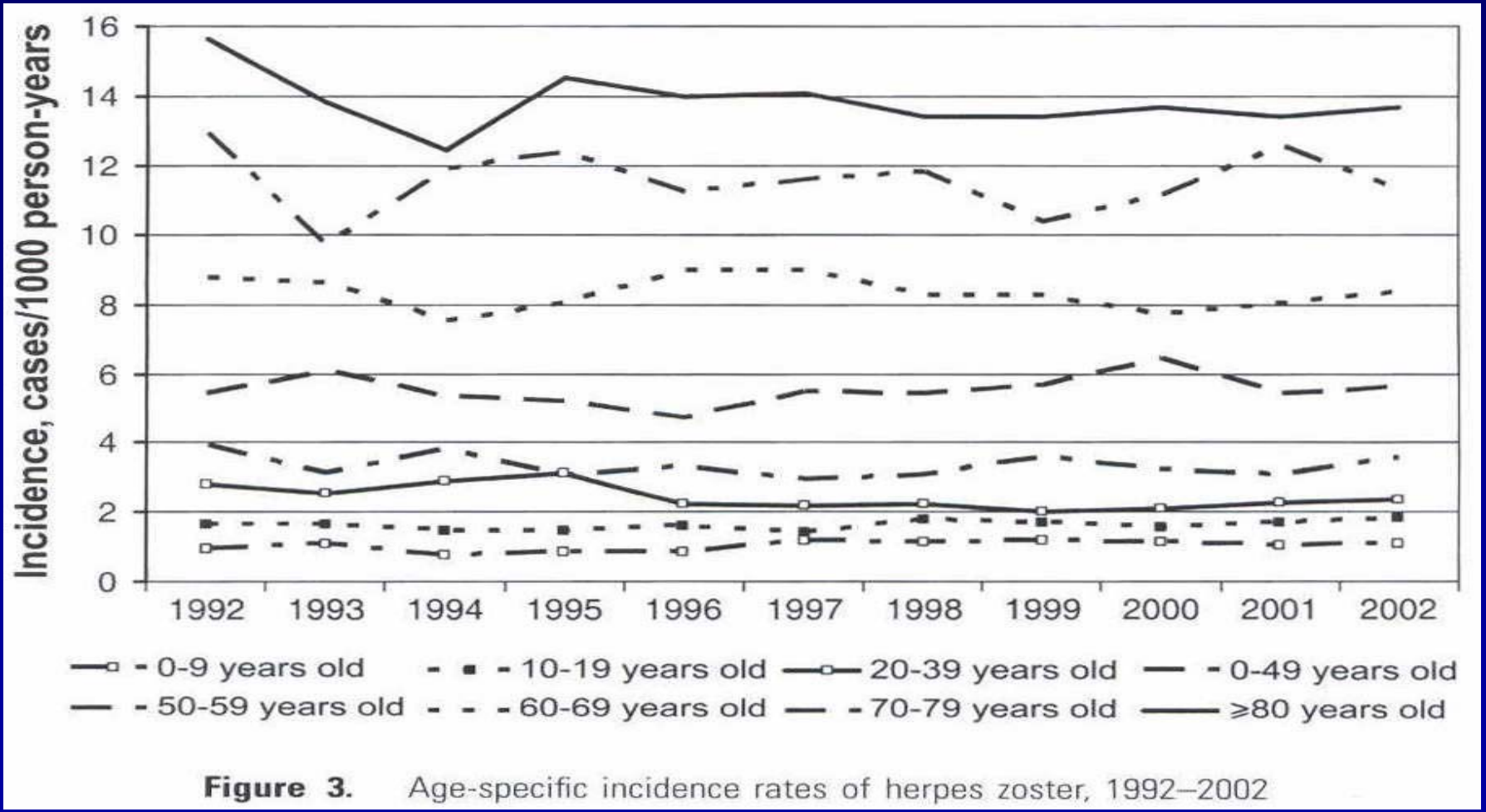


Figure 3. Age-specific incidence rates of herpes zoster, 1992–2002

Jumaan AO et al. J. Infect Dis 2005;191:2002-2007

Risk Factors for Herpes Zoster

- **Cellular immunosuppression**
  - **HIV/AIDS: 29-51 cases per 1000 person-years**
  - **Lymphoproliferative cancers: 5-14% of patients with Hodgkin's disease, non-Hodgkin's lypmphoma, leukemia**
  - **Organ transplants: 13-55% of bone marrow transplant recipients**
  - **Systemic lupus erythematosus: 16-22 cases per 1000 person-years**
  - **Immunosuppressive treatments: chemotherapy, radiation therapy, corticosteroids**

Thomas SL et al. Lancet Infect Dis 2004;4:26-33; Schmader, KE. In: Varicella-Zoster Virus, Arvin&Gershon, eds. Cambridge University Press 2000:2220-246

Risk Factors for Herpes Zoster

- **Sex**
  - **Increased risk in females? – multiple studies with conflicting results**

Incidence per 1000 person-years in placebo group, Shingles Prevention Study

Male	Female
10.65	11.79

- **Race**
  - **Decreased risk in blacks compared to whites?**

Adjusted risk ratio blacks vs. whites, prospective cohort studies

Country	Adj. RR	95% CI
US	0.35	0.24-0.51
UK	0.42	0.21-0.97

Oxman et al. NEJM. 2005;352:2271-84; Thomas SL et al. Lancet Infect Dis 2004;4:26-33; Schmader KE et al. J Am Geriatr Soc 1998;46:973-977.

Risk Factors for Herpes Zoster

- **Psychological Stress**
  - **Increased risk with stress?**
  - **One case-control study**

Adjusted odds ratio for effect of stressful life events

Month before rash onset	Adj. OR	95% CI
Two	2.6	1.1-6.3
Six	2.0	1.1-3.9

  - **One cohort study**
  - **Adj. RR stressful life events**
  - **1.38, 95% CI 0.96-1.97**

- **Physical trauma**
  - **Increased risk after trauma?**
  - **One case-control study**

Adjusted odds ratio for effect of physical trauma, site as rash

Month before rash onset	Adj. OR	95% CI
One	8.0	2.2-28.7
Six	12.0	1.5-97.6

Thomas SL et al. BMJ 2004;328:439;
Schmader KE et al. J Am Geriatr Soc 1998;46:973-977;
Schmader KE et al. J Am Geriatr Soc 1990; 38:1188-1195.

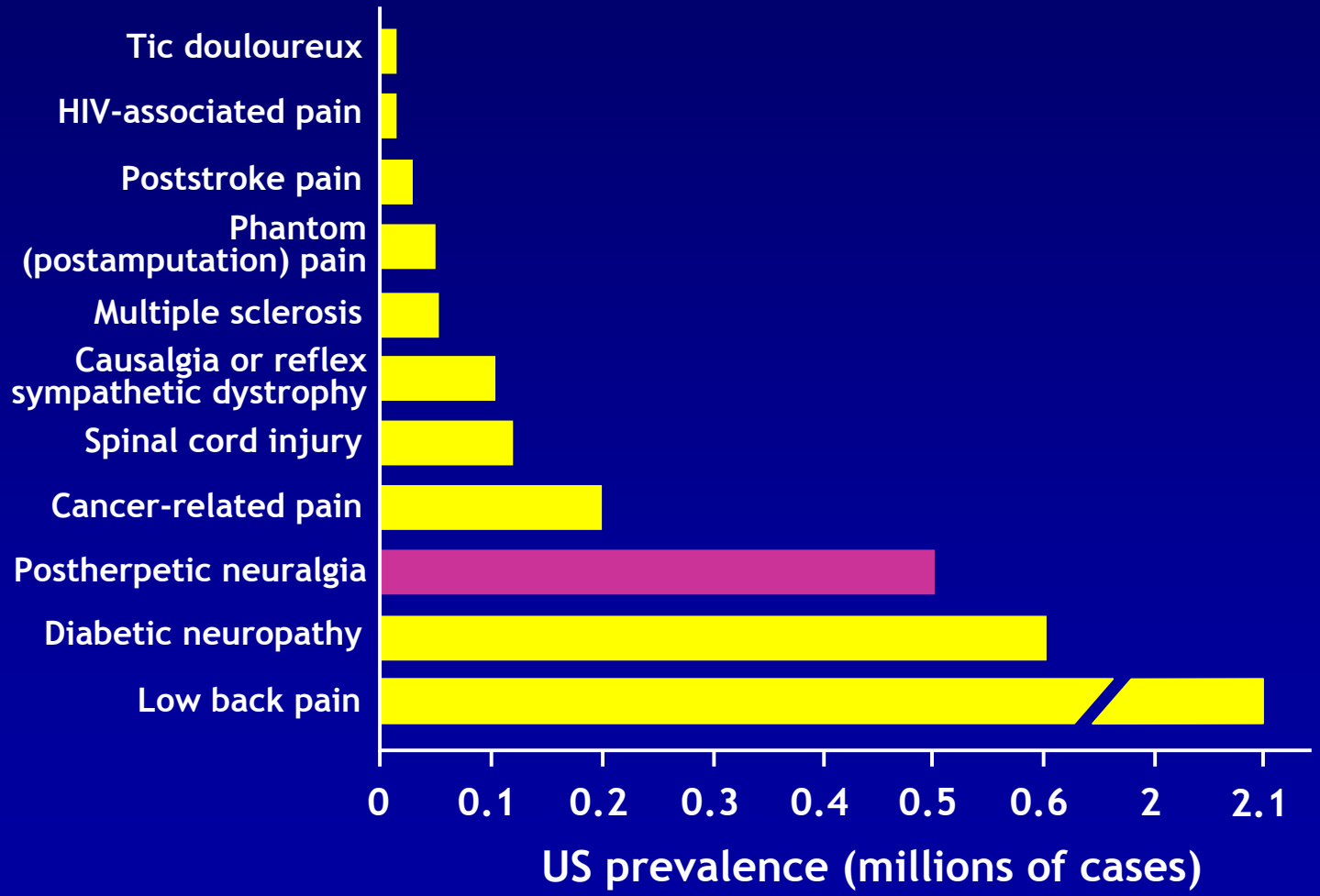
Postherpetic Neuralgia (PHN): Definitions

- **Variable definitions in the literature by time from rash onset (e.g., 30, 60, 90, 120, 180 days) and pain intensity (any pain vs. clinically meaningful pain ratings)**
- **Recent definitions focus on any pain 90 or 120 days after rash onset**

Cunningham AL, Dworkin RH. BMJ. 2000;321:778-779; Dworkin RH, Portenoy RK. Lancet. 1994;343:1648

Arani RB, et al. Stat Med 2001;20:2429-2439; Desmond RA, et al. J Pain Symptom Manage 2002;23:510-516

Sources of Neuropathic Pain



Bennett G. Hosp Prac. 1998;33:95-98;101-104;107-110.

Summary Estimates of the Proportion of Zoster Patients Over 50 Years Old with Pain After Rash Onset Enrolled in Major Antiviral Trials

Days After Rash Onset	Percent of Patients with Pain	
	Placebo	Antiviral
30	68	49-57
60	60	50
90	55	25-35
120	46	29
150	42	26
180	40	15-26

Dworkin&Schmader in Herpes Zoster and Postherpetic Neuralgia, 2nd ed., 2001 Watson&Gershon, editors; Beutner et al., 1995; Wood et al., 1996; Dworkin et al., 1998

Incidence of PHN in the Placebo Group in the Shingles Prevention Study

642 herpes zoster (HZ) cases in 19,247 placebo recipients

Days from Rash Onset	No. (%) HZ cases with PHN*	Incidence per 1000 Person-Yr
30	196 (30.3)	3.39
60	113 (17.6)	1.96
90	80 (12.5)	1.38
120	54 (8.4)	0.93
180	33 (5.1)	0.57

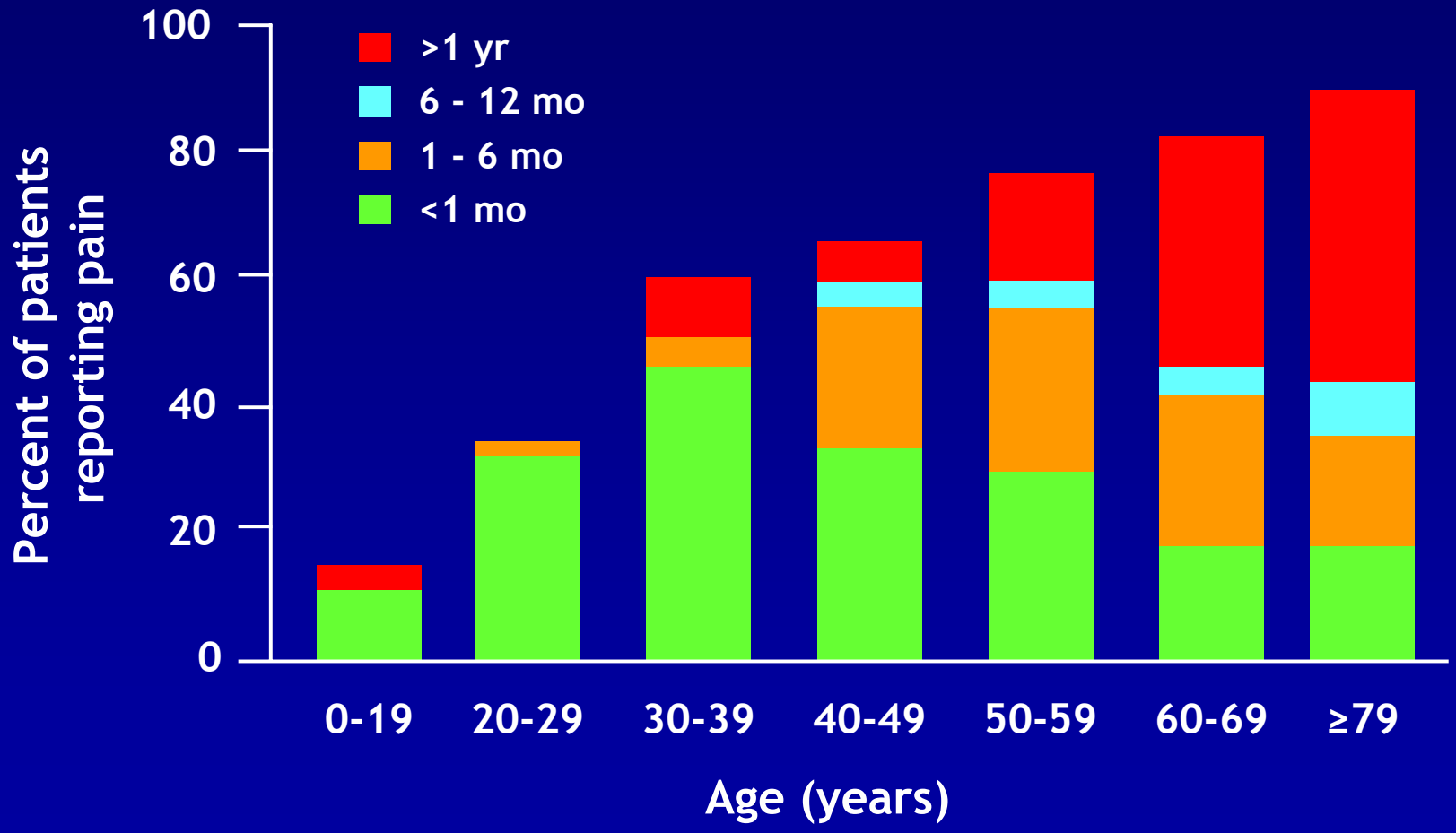
For study endpoint, PHN was defined as the pain and discomfort associated with HZ rated as 3 or more on a worst pain scale ranging from 0 (no pain) to 10 (worst pain you can imagine) persisting or appearing more than 90 days after the onset of HZ rash.

Oxman et al. NEJM. 2005;352:2271-84

Increasing Age is the Most Powerful Risk Factor for Postherpetic Neuralgia

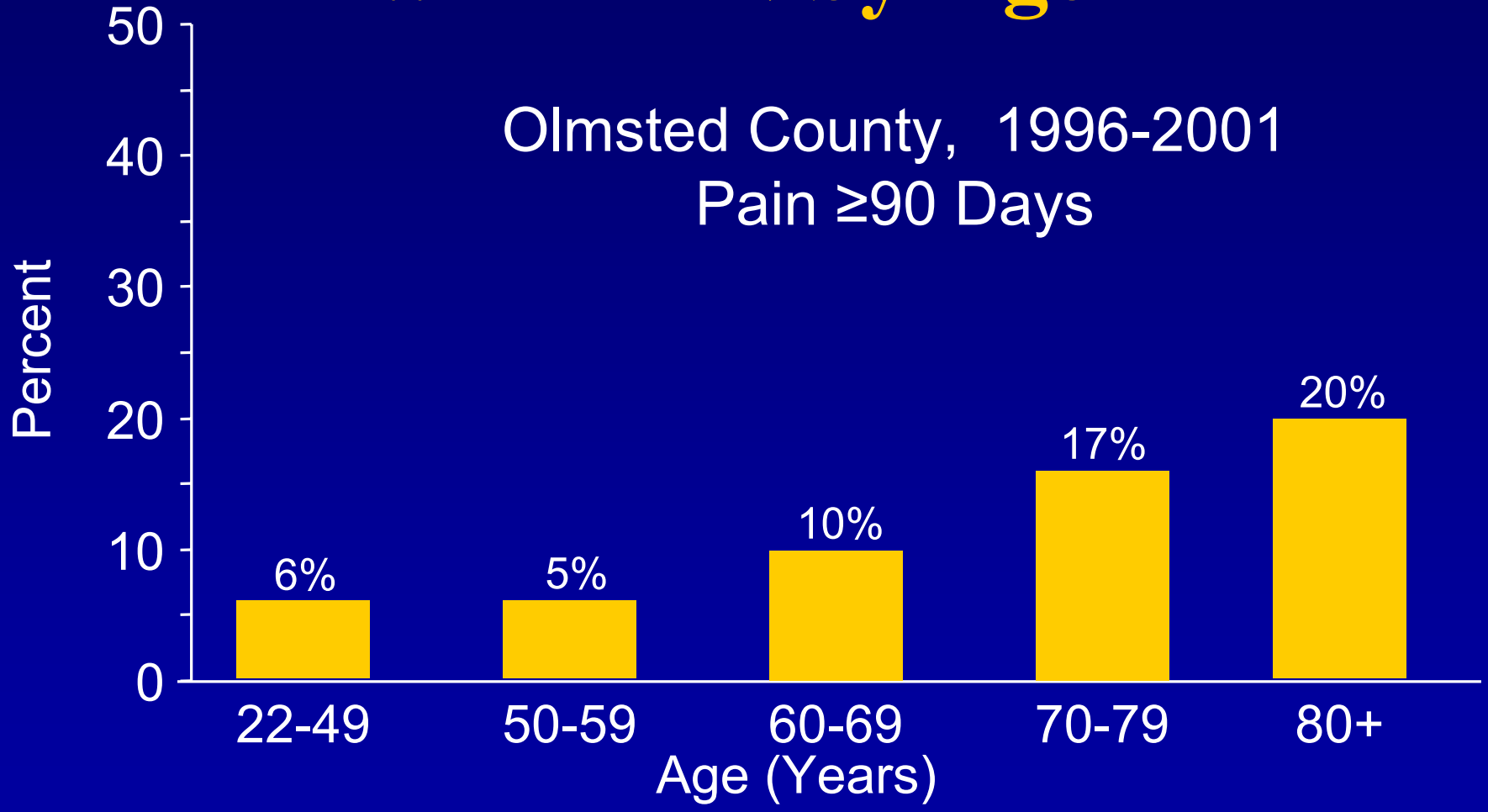
Hope-Simpson RE. J Royal Coll Gen Pract 1975;25:571-5.
Choo PW, et al. Arch Intern Med 1997;157:1217-24.

Prevalence of PHN and Duration of Pain Associated With PHN Increase With Age



Kost R et al. N Engl J Med. 1996;355:32-42.

Proportion of HZ Cases (n=1655) with PHN by Age



Yawn B et al, Olmsted Medical Center, Mayo Clinic, Merck Research Laboratories. ACIP Zoster Working Group meeting 2.06

Other Risk Factors for Postherpetic Neuralgia

- Severity of acute pain
- Severity of acute rash
- Painful prodrome
- Female sex

- Age ≥60 yrs + severe acute pain + severe rash + prodrome + female sex:
  - Positive predictive value = .47
  - Negative predictive value = .88

Jung BF. Neurology. 2004;62:1545-1551.

Complications of Herpes Zoster

Common

- Acute and Postherpetic neuralgia
- Ocular complications of Ophthalmic zoster
- Scarring
- Bacterial superinfection

Less common

- Cutaneous dissemination
- Herpes gangrenosum
- Pneumonitis
- Hepatitis
- Encephalitis
- Motor neuropathies
- Myelitis
- Hemiparesis (granulomatous CNS vasculitis)

Gnann J et al. N Engl J Med. 2002;347:340-346.

Herpes Zoster Ophthalmicus

- About 15% of zoster cases involve the ophthalmic division of the trigeminal nerve
- Keratitis, conjunctivitis, scleritis, iritis, anterior uveitis, retinitis
- Without antiviral therapy, 50-70% of patients with HZO develop ocular complications
- Can result in chronic ocular complications and reduced vision, even blindness

McPherson R. J Am Optom Assoc. 1997;68:527-538.

Complications of Herpes Zoster

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Gnann J et al. N Engl J Med. 2002;347:340-346.

Pain is the Cardinal Problem Posed by Herpes Zoster in Older Adults -- *Acute and Chronic Pain*

Acute Herpes Zoster Pain: A Source of Significant Morbidity

- Prospective study of herpes zoster pain and its relationship to physical, role, social, and emotional functioning in 110 patients with herpes zoster, 72% of patients ≥50 years old.
  - Pain burden a product of pain intensity by duration
- Greater pain burden was associated with poorer physical functioning, increased emotional distress, and decreased role and social functioning
- 42% of patients report that acute zoster pain is “horrible” or “excruciating”
- HZ pain had interfered "quite a bit" or "extremely" with physical (14.6%), role (21.8%), and social functioning (26.3%) of patients

Katz J et al. Clin Infect Dis. 2004;39:342-348.

Impact of Acute Herpes Zoster on Mean SF-36* Domains Relative to Other Diseases

SF-36 Domain	HZ 2 weeks	HTN	CHF	DM	MI	Depression
Physical Function	64	73	48	68	69	72
Role-Physical	18	62	34	57	51	44
Bodily Pain	34	72	63	69	73	59
General Health	72	63	47	56	59	53
Vitality	44	58	44	56	58	40
Social Function	50	87	71	82	85	57
Role-Social	46	77	64	76	73	39
Mental Health	67	78	75	77	76	46
Number Patients	46	2089	216	541	107	502

*Lower SF-36 scores indicate lower quality of life

Lydick E et al. Qual Life Res 1995;4:41-45.

Impact of PHN on Quality of Life in Older Adults

Physical	Psychological
• **Chronic fatigue** • **Anorexia** • **Weight loss** • **Physical inactivity** • **Insomnia**	• **Depression** • **Anxiety** • **Difficulty concentrating**
Social	**Functional**
• **Decreased social gatherings** • **Change in social role**	• **Interfere with basic and instrumental activities of daily living** – **Dressing, Bathing, Eating, Mobility** – **Travelling, Cooking, Housework, Shopping**

Schmader KE. Clin Infect Dis2001;32(10):1481-6

Impact of PHN on Quality of Life in Older Adults

- **In a pain clinic in Liverpool, 59% of PHN patients were prevented from pursuing their usual activities for up to 16 years, with the average being 1.4 years**
- **In a large case series of patients with herpes zoster from a dermatology clinic, insomnia (25%) and feeling helpless and depressed (20%) were common problems related to herpes zoster pain**

Davies L et al. Pharmacoeconomics. 1994;6:142-148.
Goh C et al. Int J Dermatol. 1997;36:667-672.

Impact of PHN on Quality of Life in Older Adults

- **Clinical trial of acyclovir vs. valacyclovir in 1,141 zoster patients ≥ 60 years of age**
  - **HRQL measure was the Nottingham Health Profile (NHP)**
  - **Zoster pain at 8 weeks after rash onset significantly interfered with the energy, sleep and global quality of life dimensions of the NHP**
  - **The magnitude of interference increased significantly as pain severity increased.**
- **Prospective observational study of 121 outpatients ≥ 60 years of age with HZ**
  - **Zoster Brief Pain Inventory, a zoster-specific measure of pain and interference with activities, correlated with the SF-12 and EuroQOL HRQL measures and an activities of daily living (ADL) questionnaire.**
  - **Pain at 35 days and 70 days after rash onset significantly interfered with multiple ADLs, reduced HRQL, and impaired mental and physical health**

Mauskopf J et al. Quality Life Res 1994;3:431-435.
Coplan PM et al. J Pain 2004;5:344-356.

Impact of PHN on Quality of Life in Older Adults

- **Mail survey of persons aged >65 years with PHN recruited via advertisements in 24 US newspapers (n = 385 respondents)**
  - **Survey addressed pain intensity, pain interference using a 0-10 scale (10 most interference), and health-related quality of life using the EuroQoL health measure [EQ-5D] and a global rating scale.**
  - **Mean (+/-standard deviation) duration of PHN was 3.3 (+/-4.0) years**
  - **Mean pain interference with general activity, mood, relations with other people, sleep, and enjoyment of life was 3.7 (+/-3.1), 4.3 (+/-2.9), 3.0 (+/-2.8), 3.8 (+/-2.9), and 4.5 (+/-3.1), respectively.**
  - **Mean EQ-5D health index score was 0.61; respondents rated their overall health as 65.7 (+/-21.1) on a 100-point scale.**

Oster G. et al. Journal of Pain. 6(6):356-63, 2005